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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,767	06/19/2001	Arthur Charles Ley	DYX-012.1 US	2306
26161	7590	07/14/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			PATTERSON, CHARLES L JR	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 09/884,767	Applicant(s) LEY ET AL.	
	Examiner Charles L. Patterson, Jr.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 November 2003 and 03 May 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4,5,50 and 51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,50 and 51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/3/04 has been entered.

Claims 1-2, 4-5 and 50-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a combination written description and enablement rejection. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

As discussed in the previous rejection, there is not seen to be justification for the general formula of claim 1 in the instant specification. The specification states on page 44 that "an amino acid was regarded as preferred at a given position in the sequence if it occurred in five or more isolates". It is not seen that applicants have justification for arbitrarily picking 5 occurrences to make a general formula. If applicants are to put forward a general rule they should have some justification for it other than an arbitrarily picked number of 5 occurrences using the specific conditions in the examples. In the amendment filed 11/20/03, applicants argue that, as discussed in the specification on pages 21-22, a "complete random library to

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be scanned for enterokinase cleavage activity was designed to allow for any amino acid except for cysteine to occur at each position...[and that] in such a random library, the likelihood of a particular amino acid being present at a particular position...is...5.2%". In their screening assay, "Applicants obtained 90 isolates...[and i]f an amino acid was present at a particular position in 5 or more of the 90 isolates, this is greater than a 5.2% chance of the amino acid occurring at that position randomly...[and indicates] that such an amino acid may play a role in cleavage by an enterokinase". The teaching in the paragraph referred to spanning pages 21-22 is that the region tested "consisted of 13 consecutive amino acids". Pending claims 1, 2, 4-5 and 50-51 contain only 7 amino acids, not 13, and therefore it is not seen how the discussion of pages 21-22 enables one to include the amino acids found 5 or more times in the general formulae of the instant claims. There were nearly twice as many amino acids in the phage library tested as are present in the instant claims and these additional amino acids may well have some effect on the percentage occurrence of a particular amino acid at a particular position. The examiner stated in the advisory action mailed 12/11/03 that this argument "may have merit, but it was not further considered because applicant has not overcome the 112 first paragraph rejection". The argument has now been considered.

In the amendment filed 11/20/03, applicants further refer to pages 43-44 which states that "only four amino acids were not observed in any of the isolates at the P<sub>1</sub>' position following Asp-Arg, among those isolates sequenced: Lys, Pro, Arg and Cys (which was not permitted in the 13-mer variable portion when the substrate phage library was generated)". They then go on to quote from these pages that "[t]he absence of any phage isolates exhibiting these amino acids at the P<sub>1</sub> position does not mean that an EK recogni-

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tion sequence...having Lys, Pro, Arg or Cys at the...[P<sub>1</sub>] position will not be cleaved; rather it indicates that such recognition sequences will be cleaved less efficiently than recognition sequences having the other amino acids at the Xaa(P<sub>1</sub>) position" and they state that "it is clear that the Xaa<sub>5</sub> position of the formula in claim 1 can be any amino acid". The examiner does not agree. Applicants have found absolute no instances of the Xaa<sub>5</sub> position being Lys, Pro, Arg or Cys and it is maintained that absent convincing proof to the contrary, these residues should not be allowed at position Xaa<sub>5</sub> in the formulae of the instant claims.

In the Remarks contained in the amendment filed 5/3/04 and the 37 CFR § 1.132 declaration, it is argued that the claims should not be required to be limited to the requirements discussed on page 33, lines 7-17 as to an "86-mer fusion protein having tandem ligand recognition sequences", etc., as discussed by the examiner on page 3 of the final rejection mailed 6/4/03. The examiner has read these arguments and this part of the rejection is hereby dropped.

It is maintained that the instant claims are not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons discussed *supra*.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR

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1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see

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<http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.  
Primary Examiner  
Art Unit 1652

Patterson  
July 9, 2004